Original Research Article

Comparison of analgesic effect of different doses of intrathecal nalbuphine hydrochloride with bupivacaine and bupivacaine alone for lower abdominal surgeries

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Abstract

Background: Nalbuphine is a opioid, structurally related to oxymorphine, highly lipid soluble opioid with an agonist action at the K- opioid receptor and antagonist activity at the μ receptor. **Aim:** To compare the characteristics of Nalbuphine effects with different doses with bupivacaine and bupivacaine alone in subarachnoid block for patients undergoing elective lower abdominal surgeries. **Methods:** A double blind prospective randomized control clinical study was conducted on120 patients of 18 to 60 years age, either sex and American society of anaesthesiologist (ASA) Ⅰ/Ⅱ undergoing elective lower limb surgeries under planned spinal anaesthesia were included and randomly allocated into 4 equal groups (n=30 each), to receive spinal anaesthesia with - 12.5mg of 0.5% heavy bupivacaine(group A), 12.5mg of 0.5% heavy bupivacaine along with 0.4mg nalbuphine (group B), 12.5mg of 0.5% heavy bupivacaine along with 0.6mg nalbuphine (group C)and 12.5mg of 0.5% heavy bupivacaine along with0.8mg nalbuphine (group D). The patients were evaluated with respect to various sensory and motor characteristics, duration of postoperative analgesia and adverse effects. **Results**: All the groups were comparable with respect to demographic profile. There was clinically significant early onset of sensory block with group C 2.5±0.78 min Vs 2.7±0.69,2.6±0.74 and 2.6±0.62 min in group A,B,D respectively with p(0.794). Time to attain highest level of sensory block with group C 7.8±0.36 min Vs 7.9±0.46,7.9±0.45 and 7.8±0.49 min in group A,B,D respectively with p(0.676). There was prolongation of duration of sensory block with group C 180±4.4 min Vs 96±6.7,164±9.9,187±2.4 min in group A,B,D groups respectively with p(<0.001). There was significant prolongation of motor blockade with group C 171.2±14.2 min Vs 164.4±12.8, 166.8±15.7, 172.5±11.1 min in A, B, D groups respectively with p(0.08). Total duration of complete analgesia with group C is 286.4±13.6 min Vs 182.6±6.72, 240.2±13.87, 292.3±17.5 min in group A,B,D respectively. The present study shown that intrathecal doses of nalbuphine namely 0.4 &0.8 mgs along with 0.6 mg to find out the optimal intrathecal dose which has maximal duration of post op analgesia with minimal adverse effects. Overall there was less adverse effects in group C patients with 0.6mg Nalbuphine as an adjuvant to 0.5/. heavy bupivacaine in spinal anaesthesia. **Conclusion:** 0.6 mg Nalbuphine as an adjuvant to spinal bupivacaine is more effective in terms of duration of sensory and motor blockade, postoperative analgesia and having less side effects. Nalbuphine provide very good quality of analgesia and prolongs duration of analgesia intraoperative and postoperative period. Adverse effects of Nalbuphine are minimal and well manageable. It provides stable hemodynamic. It does not produce respiratory depression. Dosage up to 0.8mg of nalbuphine may be used without any major adverse effects.

Key words: Nalbuphine, Bupivacaine, Subarachnoid block, Hemodynamic changes, Respiratory depression

Introduction

Spinal anaesthesia is most popular regional anaesthesia technique. Spinal anaesthesia is advantageous in that it use small dose of anaesthetic, is simple to perform and offers rapid onset of action, reliable surgical analgesia and good muscle relaxation[1]. The discovery of opioid receptors in the spinal cord have opened new avenues for relief of pain, both in intra-operative and post-operative periods by administering them through intrathecal as well as through epidural route[1,2].

Nalbuphine is an opioid, structurally related to oxymorphone. It is highly lipid soluble opioid with an agonist action at the kappa and antagonist action at the mu /depression etc. because of its action at kappa receptor various studies have been evaluated to know the effective intrathecal dose of nalbuphine. Hence an attempt has been made to evaluate the optimum effective dose of nalbuphine with minimal adverse effects[3]. Nalbuphine with doses of 0.4 mg. 0.6 mg & 0.8 mg are added to 0.5% hyperbaric bupivacaine in spinal anaesthesia to know the efficacy, duration of analgesia, incidence of side effects and complications ifany. Is less likely to cause adverse effects like puritis, nausea, and vomiting, urinary retention.

Material and methods

A double blind prospective randomized controlled clinical study was conducted on 120 adult patients in the age group of 18 – 60 years, posted for elective lower abdominal surgeries at Govt. General Hospital, Kurnool Medical College, Kurnool. from the period May 2017 - August 2018.

Study design

A double blind prospective randomized controlled clinical study.

Source of data

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In patients posted for elective lower abdominal surgeries at Govt. General Hospital, Kurnool Medical College, Kurnool. Study was conducted on 120 patients

Study population
Population based on following criteria.

Inclusion criteria
1. ASA grade 1 &2patients.
2. Age group of18–60yrs.
3. Patients giving valid informed consent.
4. Patients scheduled to undergo elective lower abdominal surgeries under subarachnoid block.

Exclusion criteria
1. Patient refusal.
2. Localized skinsepsis.
3. Patients belonging to ASA grade 3 andgrade4.
4. Cardiac disease, heart blocks, dysarhythmias, patients on beta blockers, & alpha antagonists.
5. History of drug allergy.
6. Gross spinal abnormality.
7. Haemorrhagicdiathesis.
8. Neurological involvement/diseases.

Procedure
Group Division
Study group A – 2.5 ml of 0.5% Bupivacaine heavy (12.5mg) + 1ml of 0.9%NS to a total volume 3.5ml.
Study Group B – 2.5 ml of 0.5% bupivacaine heavy (12.5mg) + 0.4mg Nalbuphine diluted to 1cc NS to a total volume of 3.5ml
Study Group C – 2.5 ml of 0.5% Bupivacaine heavy (12.5mg0 + 0.6mg nulbuphine diluted to 1cc NS to a total volume of 3.5ml.
Study Group D– 2.5 ml of 0.5% Bupivacaine heavy(12.5mg)+0.8mg nulbuphine diluted to 1cc NS to a total volume of3.5ml.

Preoperative preparation
All patients are preloaded with 10ml/kg of ringer lactate and all patients premedicated with 4mg of Ondansetron and Ranitidine 50 mg intravenously

Monitoring
The monitors connected to the patient included electrocardiogram (ECG), Non-invasive blood pressure (NIBP), Pulse oximeter (SpO2). Preoperatively base line parameters like heart rate, blood pressure, respiratory rate and oxygen saturation were recorded. Sterile precautions were taken to avoid dangerous complications by introducing infection from outside to inside.
Subarachnoid block was performed with patient in Left lateral position. Under strict aseptic precautions, Lumbar puncture was performed with 25G Quincke"s type spinal needle at L3 - L4 or L4 - L5 intervertebral space using midline approach. Following free flow of CSF, drug was injected into subarachnoid space.

Vital parameters
HR, SBP, DBP, MAP were recorded every 5min up to 30min, thereafter every 15min up to 60min and then every 30 min up to 120min.

Assessment of sensory blockade
The onset of sensory block was tested by pin prick method using a 23G hypodermic needle along mid-clavicular line. The time of onset was taken from the time of injection of drug into subarachnoid space to loss of pin prick sensation at T8. The highest level of sensory block and time was noted. The time for 2 dermatomal segment regression of sensory level was noted. Observations were made at 0,1,3, 5,10,15,20,30,45,60,90 and 120 min after injection of the drug. The following side effects like nausea, vomiting, pruritis, hypoxemia, respiratory depression, hypotension, and bradycardia were observed and recorded in both intra operative and postoperative period.

Visual Analogue Scale (VAS)
Since the perception of pain is highly subjective, this variable was standardized by using data from VAS. VAS consists of 10cm line anchored at one end by a label such as no pain and at the other end by a label such as the 'worst pain imaginable' or pain as bad as can be. The patient simply marks the line to indicate the pain intensity and the provider then measure the length of the line to mark on a point scale.

The duration of analgesia
The duration of analgesia was calculated from the intrathecal injection of drug to first analgesic request by the patient or VAS was 4 or more. VAS was assessed every 30 min up to 300 min after SAB or until VAS ≥ 4. When VAS≥4 or first analgesic request by patient, rescue analgesic in the form of injection Diclofenac 75 mg IM. Was given and the study ended.

Statistical analysis
Demographic data was entered into excel and analyzed using statistical package for social science (SPSS) version 21.Quantitative variables were expressed in mean and standard deviation. The association between the groups were tested using unpaired t- test for inter group comparisons and analysis of variance (ANOVA) for overall comparisons. Categorical data was expressed in frequencies and association was tested using chi-square statistic value less than 0.05 was considered significant.

Results & discussion
The present study was done by using doses of 0.4mg,, 0.6mg, & 0.8mg taking into consideration the studies done and published articles. It was found that 0.2 mg of nalbuphine has been proved that it does not prolong post-operative analgesia[5].
Hence an effort has been made to compare 2 popular intrathecal doses of nalbuphine namely 0.4 & 0.8 mg along with 0.6 mg to find out the optimal intrathecal dose which has maximal duration of post-operative analgesia with minimal adverse effects.3 doses of nalbuphine has also been compared to plain bupivacaine to authenticate the analgesia effects of Nalbuphine in post-operative period. Bupivacaine group with no intrathecal Nalbuphine is taken as control group.
Mukherjee *et* al[5]. Were compared different doses of intrathecal nalbuphine in 100 patients undergoing orthopedic lower limb surgeries under spinal anesthesia. They used different doses of nalbuphine 0.2, 0.4, and 0.8 mg added to 0.5% bupivacaine and they concluded that 0.4 and 0.8 mg have significant prolong the duration of analgesia but adverse effect higher with 0.8 mg dose. Jyothi et.al[7], revealed 0.8mg as effective (optimum) dose but in the studies where 0.8mg has been compared with higher doses of nalbuphine like 1.2 & 2.4 mg. In this study, they compared morphine 0.2 mgadded to hyperbaric bupivacaine with different dose of intrathecal nalbuphine 0.2, 0.8, and 1.6 mg added to hyperbaric bupivacaine and concluded that nalbuphine 0.8 mg have significant prolonged duration with minimal side effects, but nalbuphine 1.6 mg did not increase efficacy but increased incidence of adverse effects. Tiwari et al[6] were compared intrathecal nalbuphine 0.2 and 0.4 mg added to hyperbaric bupivacaine with bupivacaine alone. They concluded that prolonged duration of analgesia was seen in nalbuphine 0.4 mg without adverse effects.
The patients studied across the group were found statistically insignificant with respect to age, sex, height, weight and duration of surgery. The types of surgeries performed were almost identical in four groups. These parameters were kept identical in four groups to avoid variations in the intra operative and post-operative outcome of the patients.
The onset of sensory block in Group A is 2.7 min, in Group B 2.6min; Group C 2.5 min; Group D 2.6 min. The onset in nalbuphine groups in earlier when compared with plain bupivacaine but it is not

statistically significant. These results are similar to Kumaresanet.al[8], where the onset of sensory block was around 3 minutes.

In another study done by Jyothi et.al[7] the onset of sensory block was around 3.4 to 3.6 min. In study by Avinash B Pawar et al[9], the onset of sensory block in nalbuphine group was around 2.92 ± 0.85 min similar to our study. The differences in time of onset in the above study was due to variation in the volume of bupivacaine used, total volume of injected drug, type of patients selected.

Table 1: Distribution of the patients by Time of onset of sensory block

a. Overall comparison of mean

Group	Time of onset of sensory block		p-value
	Mean	Standard deviation	
A	2.7	0.69	0.794 (NS)
B	2.6	0.74	
C	2.5	0.78	
D	2.6	0.62	

b. inter-group comparison ofmean

Comparison of mean between	p-value
Group A vs Group B	0.519 (NS)
Group A vs Group C	0.339 (NS)
Group A vs Group D	0.517 (NS)
Group B vs Group C	0.749 (NS)
Group B vs Group D	0.955 (NS)
Group C vs Group D	0.689 (NS)

Time to attain highest level of sensory block in our study was Group A 7.9 min, Group B 7.9 min, Group C 7.8 min, Group D 7.8 min. There was no statistical significance in attaining highest level of sensory block among the four groups. Similar results were observed by Kumkum Gupta et al[10], who observed the time taken for highest level of sensory block was 7.1 to 7.4 min.

Table 2: Distribution by Time to attain highest level of sensory block (mins)

Time of attain highest level of sensory block (mins)			
Group	Mean	Standard deviation	p-value
A	7.9	0.46	0.676 (NS)
B	7.9	0.45	
C	7.8	0.36	
D	7.8	0.49	

Time for two segment regression in Group A was 96±6.7 min, Group B 164 ± 9.9 min, Group C 180 ± 4.4 min, Group D 187 ± 2.4 min. The time for two segment regressions was prolonged in Group B, C and D when compared with GroupA (plain bupivacaine) among nalbuphine groups; the time for two segment regression was prolonged in Groups C & D when compared with Group B which is statistically significant. When Group C compared with Group D the time for two segment regression was prolonged in Group D, but it was not statistically significant. These results were similar to other studies done by Mukherje A et.al[5]. Who reported the time for two segments repression was around 118 ± 6.8 min to 154 ± 6.0 min. The present study results are in accordance with studies done by Shela Shakooh et.al[11]., (2014), who found that two segment regression time of sensory blockade in nalbuphine group was prolonged as compared to control group ($P < 0.05$) which was statistically significant

Table 3: Distribution by Time for Two dermatomal segments regression of Sensory blockade (min)

Time for Two dermatomal segments regression of sensory blockade (min)			
Group	Mean	Standard deviation	p-value
A	96.7	6.71	<0.001 (S)
B	164.8	9.93	
C	180	4.04	
D	187.6	2.40	

Hemodynamic parameters

Intrathecal nalbuphine along with Bupivacaine used in the study has minimal hemodynamic effects. The physiological changes in the hemodynamic Parameters are due to sympathetic block due to spinal anaesthesia which causes fall in blood pressures systolic, diastolic and mean arterial pressures. Intrathecal nalbuphine has no effect hemodynamic parameters.

In the present study, there was no statistically significant difference in the heart rate, systolic blood pressure, diastolic pressure and mean arterial blood pressure at different time intervals in the A and B groups in the perioperative period.

According to studies done by Apeksha A.Patwa et al[12]., even at higher doses did not show any significant difference in hemodynamic parameters probably due to sympathetic sparing effect of nalbuphine. On inter and intra group comparison, there were no significant changes in pulse rate at any time during intra operative period. However the fall in blood pressure did occur but was not of grade of hypotension i.e. change in blood pressure of < 20% of base line value.

Table 4: Distribution of patients by mean heart rate

Mean heart rate	Group A	Group B	Group C	Group D	p-value
0 min	89±7.27	89±6.2	91±6.4	91±6.2	0.425 (NS)
1 min	95±7.3	95.1±6.19	97.3±6.42	97.2±6.18	0.338 (NS)
2 min	85±7.27	85.1±6.19	87.3±6.42	87.2±6.18	0.337 (NS)
3 min	83±7.27	83.1±6.19	85.3±6.42	85.2±6.18	0.337 (NS)

5 min	79±7.27	79.1±6.19	81±6.4	81.2±6.18	0.399 (NS)
10 min	76±7.3	76.1±6.19	78±6.4	78±6.2	0.448 (NS)
15 min	74±7.3	74±6.2	76±6.4	76±6.2	0.426 (NS)
20 min	85±7.27	85±6.2	87±6.4	87±6.2	0.425 (NS)
30 min	87±7.27	87±6.2	89.3±6.42	89±6.2	0.355 (NS)
60 min	90±7.27	90±6.2	92±6.4	92±6.2	0.425 (NS)
90 min	97±7.3	97.1±6.19	99.3±6.42	99±6.2	0.377 (NS)
120 min	98±7.27	98.1±6.19	100±6.42	100±6.2	0.448 (NS)

Table 5: systolic blood pressure (SBP) in four groups at different time intervals

Mean SBP	Group A	Group B	Group C	Group D	p-value
0 min	123±4.57	122±5.14	120±7.4	119±8.8	0.09 (NS)
1 min	125±5.12	125±5.6	124±7.6	123±8.5	0.625 (NS)
2 min	112±7.1	111±6.6	110±7.4	109±8.8	0.452 (NS)
3 min	111±6.4	109±6.6	108±7.2	107±8.2	0.167 (NS)
5 min	104±6.39	103±6.7	102±7.4	101±8.8	0.435 (NS)
10 min	99±7.4	98±8.8	96±7.1	95±8.6	0.203 (NS)
15 min	94±7.3	93±8.9	92±7.4	91±8.8	0.521 (NS)
20 min	96±7.00	95±8.3	94±7.4	93±8.8	0.497 (NS)
30 min	102±7.35	101±8.0	99±7.3	98±8.7	0.189 (NS)
60 min	111±6.6	110±7.4	109±7.4	108±8.8	0.460 (NS)
90 min	113±6.4	112±7	111±6.4	110±8.7	0.411 (NS)
120 min	116±6.8	115±6.43	113±7.4	112±8.8	0.124 (NS)

Table 6: Distribution of participants by mean diastolic blood pressure (DBP)

Mean DBP	Group A	Group B	Group C	Group D	p-value
0 min	84±8.8	83±6.1	82±7.92	80±7.9	0.229 (NS)
1 min	86±8.9	85±7.9	84±6.5	81±6.3	0.06 (NS)
2 min	77±7.9	78±8.1	76±7.9	74±6.2	0.211 (NS)
3 min	75±7.6	76±7.4	73±5.9	72±6.4	0.101 (NS)
5 min	69±8	70±7.8	66±7.9	68±7.2	0.228 (NS)
10 min	65±8.4	66±7.9	63±7.3	61±7.4	0.07 (NS)
15 min	63±7.9	64±8.1	61±7.8	60±7.5	0.186 (NS)
20 min	65±7.9	66±7.9	63±7.2	61±7.7	0.06 (NS)
30 min	70±8.1	71±8.0	68±7.2	67±7.7	0.179 (NS)
60 min	75±7.9	74±8.1	73±7.3	70±7.8	0.08 (NS)
90 min	77±7.9	76±7.4	75±5.9	73±6.2	0.144 (NS)
120 min	78±8.1	77±8.0	75±7.6	74±6.5	0.162 (NS)

Table 7: Mean Arterial Pressure (MAP) in four groups at different time intervals

MAP	Group A	Group B	Group C	Group D	p-value
0 min	97.4±5.89	96.4±4.00	94.7±5.58	93.9±6.43	0.07 (NS)
1 min	98.9±6.34	98.2±5.66	97.1±5.62	95.2±5.10	0.07 (NS)
2 min	88.6±5.72	89.1±6.07	87.3±6.16	85.4±4.94	0.06 (NS)
3 min	87.1±5.58	87.1±5.33	85.1±5.41	84±5.00	0.06 (NS)
5 min	80.5±5.74	81.2±5.76	78±6.16	79.2±5.71	0.158 (NS)
10 min	76.3±6.08	76.6±5.60	74.2±6.2	73.1±6.15	0.08 (NS)
15 min	73.4±5.51	73.6±5.70	71.1±6.11	70.9±6.18	0.148 (NS)
20 min	75.4±5.63	75.7±5.61	73.1±5.99	72.3±6.42	0.07 (NS)
30 min	80.7±5.71	81±5.53	78.6±5.21	77.6±5.81	0.06 (NS)
60 min	87.1±5.94	85.8±6.21	84.8±5.67	83±6.3	0.07 (NS)
90 min	89±5.23	87.9±5.63	86.8±4.97	85.8±5.79	0.125 (NS)
120 min	90.5±6.45	89.6±5.27	87.7±5.44	87±5.33	0.06 (NS)

Table 8: Distribution of participants by mean oxygen saturation (SpO_2)

SpO_2	Group A	Group B	Group C	Group D	p-value
0 min	97.5±0.97	97.7±1.06	97.7±0.92	97.8±0.97	0.688 (NS)
1 min	97.8±0.97	97.7±0.92	97.7±0.94	97.6±0.96	0.881 (NS)
2 min	97.6±0.93	97.5±1.01	97.5±0.97	97.5±1.01	0.972 (NS)
3 min	97.7±0.92	97.9±0.97	97.8±0.97	97.7±1.06	0.836 (NS)
5 min	97.7±0.94	97.7±1.03	97.6±0.96	97.7±0.92	0.970 (NS)
10 min	97.6±0.96	97.6±0.93	97.5±1.01	97.5±1.01	0.957 (NS)
15 min	97.5±1.01	97.7±0.92	97.7±1.06	97.9±0.97	0.489 (NS)
20 min	97.7±0.92	97.7±0.94	97.7±0.92	97.7±1.03	1.000 (NS)
30 min	97.5±1.01	97.5±0.97	97.5±1.01	97.6±0.93	0.972 (NS)
60 min	97.9±0.97	97.8±0.97	97.9±0.97	97.7±0.92	0.826 (NS)
90 min	97.7±1.03	97.6±0.96	97.7±1.03	97.7±0.94	0.973 (NS)
120 min	97.7±1.06	97.5±1.01	97.6±0.93	97.5±0.97	0.841 (NS)

Motor block

In the present study, the time interval between injection of drug into subarachnoid space to the patient's inability to lift the straight extended leg was taken as onset of motor block. The onset of motor block in Group A was 5.1 min, Group B 5.1 min, Group C 5.0 min, Group D 4.9 min . The onset of motor blockade in Group A was similar when compared with nalbuphine Groups (B, C, D); even among nalbuphine groups the onset of motor blockade was similar with no statistical significance. This can be explained on the basis of the motor sparing effects of nalbuphine. Similar results were observed by Arghya Mukarjie et.al[20]., reported the onset of motor block was around 5.6 min also found that there was no statically significance in onset of motor blockade with different doses of nalbuphine as compared to control group. From the above studies it can be inferred that even with usage of different doses there is no change in onset of motor blockade which can be attributed to motor nerve sparing effect of nalbuphine.

In the present study the duration of motor block was assessed from the time of onset of motor block to patient's ability to lift the straight extended leg. Duration of motor blockade in Group A was 164.4±12.8 min , Group B 166.8±15.7.min , Group C 171.2±14.2 min ,and Group D 172.5±11.1 min. Among Groups B, C, D, the duration of motor block was slightly prolonged in Groups C & D when compared with Group B, but it is not statistically significant. Similar results were observed in Apeksha patwa et.al[41], where there was no statistically difference in the duration of motor blockade with different doses of Nalbuphine. In contradiction to our results the duration of motor motor blockade was prolonged in studies done by kumaresan et.al[21]., Kumkum Gupta et.al[27].

Table 9: Distribution of patients by Time for onset of motor block (min)

a. Overall coparison ofmean

Time for onset of motor block (min)			
Group	**Mean**	**Standard deviation**	**p-value**
A	5.10	0.39	
B	5.06	0.41	
C	5.04	0.38	
D	4.95	0.27	0.462 (NS)

b. inter-group comparison ofmean

Comparison of mean between	p-value
Group A vs Group B	0.723 (NS)
Group A vs Group C	0.551 (NS)
Group A vs Group D	0.100 (NS)
Group B vs Group C	0.819 (NS)
Group B vs Group D	**0.223 (NS)**
Group C vs Group D	**0.314 (NS)**

Table 10: Distribution of patients by duration of motor block (min)

c. Overall comparison of mean

Duration of Motor block (min)			
Group	**Mean**	**Standard deviation**	**p-value**
A	164.4	12.8	
B	166.8	15.7	
C	171.2	14.2	0.08 (NS)
D	172.5	11.1	

d. inter-group comparison ofmean

Comparison of mean between	p-value
Group A vs Group B	0.902 (NS)
Group A vs Group C	0.216 (NS)
Group A vs Group D	0.101 (NS)
Group B vs Group C	0.592 (NS)
Group B vs Group D	0.367 (NS)
Group C vs Group D	0.982 (NS)

VAS

Intrathecal Nalbuphine has the properties of producing prolonged analgesia both intraoperative and extended on to postoperative period.

In the present study VAS score was assessed at 150 min, 180 min, 240 min, & 300 min. It was observed that patients in Groups B,C ,D (Nalbuphine groups) when compared with Group A.(Plain Bupivacaine) showed that patients in nalbuphine group VAS was less in Group C & D compared with Group B, but it is not statistically significant, it was also observed that VAS score was less in Group D when compared with Group C but it is not statistically significant . The following result of our study are in accordance with the studies done by Tiwari,TomasGSet.al[36]., Jyothi B Shruthi Gowda et.al[19]., who observed less VAS score in nalbuphine groups when compared with control group.In the present study, the duration of effective analgesia was calculated from the intrathecal injection of drug to first analgesia request by the patient or VAS score of 4 or more. The duration of effective (complete) analgesia in Group A (plain bupivacaine) was 182.min in Group B 240.min, Group C 286.min & Group D 293.min. The duration of complete analgesia in nalbuphine groups (B, C, and D) was prolonged when compared with Group A which is statistically significant. Among nalbuphine groups the duration of completed analgesia was prolonged in groups C & D when compared with Group B which was statistically significant, When Group C was compared with Group D the duration of complete analgesia was prolonged in Group D when compared with Group C but it is not statistically significant. The present study results are in accordance with study done by Kumaresan et. Al[21].,who observed that prolonged duration of analgesia . Similar studies done by Pallavi Ahluvalia et al[44], in, Sapate M Sahu et al[35], , was observed that prolonged duration of analgesia in nalbuphine group which was statistically significant.

Table 11: VAS scoring and rescue analgesics

a. overall change with time

Group	Visual	T_{150}	T_{180}	T_{210}	T_{240}	T_{270}	T_{300}	$T_{>300}$
A	0-3	14	7	2	0			
	3-5	12	10	4	3			
	5-8	4	10	17	14			
	8-10	0	3	7	13			
B	0-3	18	16	10	6	1		
	3-5	10	12	7	8	4		
	5-8	2	2	10	14	10		
	8-10	0	0	3	2	15		
C	0-3	-	23	21	19	8	3	2
	3-5	-	7	9	9	15	10	8
	5-8	-	0	0	2	7	15	17
	8-10	-	0	0	0	0	2	3
D	0-3	-	26	23	20	12	5	0
	3-5	-	4	7	9	13	14	12
	5-8	-	0	0	1	5	11	17
	8-10	-	0	0	0	0	0	1

b. inter-group comparisons

Group	T_{150}	T_{180}	T_{210}	T_{240}	T_{270}	T_{300}	$T_{>300}$
A vs B	0.510;	0.003;	0.02;	<0.001;			
A vs C	-	<0.001;	<0.001;	<0.001;			
A vs D	-	<0.001;	<0.001;	<0.001;			
B vs C	-	0.058;	0.004;	<0.001;	<0.001;		
B vs D	-	0.005;	<0.001;	<0.001;	<0.001;		
C vs D	-	0.317;	0.559;	0.836;	0.528;	0.293;	0.592;

Table 19: Distribution of the groups by highest score on VAS

a. Overall comparison ofmean

Highest score of the VAS			
Group	**Mean**	**Standard deviation**	**p-value**
A	5.52	2.34	0.004 (S)
B	4.79	2.50	
C	3.83	2.38	
D	3.47	2.15	

b. inter-group comparison ofmean

Comparison of mean between	p-value
Group A vs Group B	0.625 (NS)
Group A vs Group C	0.03 (S)
Group A vs Group D	0.005 (S)
Group B vs Group C	0.391 (NS)
Group B vs Group D	0.135 (NS)
Group C vs Group D	0.934 (NS)

Table 12: Distribution of patients by total duration of complete analgesia (min)

a. Overall comparison ofmean

Total duration of complete analgesia (min)			
Group	**Mean**	**Standard deviation**	**p-value**
A	182.6	6.72	.001 (S)
B	240.2	13.87	
C	286.4	13.60	
D	292.3	17.50	

b. inter-group comparison ofmean

Comparison of mean between	p-value
Group A vs Group B	<0.001 (S)
Group A vs Group C	<0.001 (S)
Group A vs Group D	<0.001 (S)
Group B vs Group C	<0.001 (S)
Group B vs Group D	<0.001 (S)
Group C vs Group D	0.148 (NS)

Side effects

In the present study no patient in Group A had nausea and vomiting, two patients in group B, one patient in group C and 2 patients in Group D had nausea and vomiting which was not statistically significant (P>0.809). The present study results are in accordance with Apeksha A Patwa, et al[41],Pallavi Ahuluvalia, et al[44], Devendra Verma, Udite Naithani et al[43], who observed that there was no statistically significant difference in the incidence of nausea

and vomiting between nalbuphine and control group.

In the present study no patient in Group A had hypotension, one patient in Group B, one patient in Group C and four patients in Group D experienced hypotension which was not statistically significant

None of the patients in our study had pruritis which correlate with the studies done by Tiwari, Tomar GS et al[36], Shehla Shakoon et.al[25]. In the present study no patients had urinary retention which inaccordance with the study done by Mukherje A, Pal A et.al[20]As nalbuphine is µ- receptor antagonist, none of the patients had µ related side effect like urinary retention.

None of the patients in our study had pruritis in fact nalbuphine has anti pruritic action through kappa agonistic activity -. Similar results were observed in studies done by Apeksha A Patwa et.al[41],.

None of the patients in our study developed respiratory depression which correlates with the studies done by Argha Mukherjee A Pal et .al[20]**.,** Nalbuphine exhibits ceiling effect for respiratory depression. Since respiratory depression in predominantly µ receptor mediated effect and nalbuphine is a µ receptor antagonist, respiratory depressant effect is expected to be attenuated by nalbuphine. Nalbuphine exhibits ceiling effect on respiratory depression which is proved in the study done by Romagnoli and Keats etal[86].

Table 13: Distribution by side effects observed in the groups

Side effects	Group A	Group B	Group C	Group D	p-value
Nausea, Vomiting	0 (0%)	2 (6.67%)	1 (3.33%)	2 (6.67%)	0.809; NS
Urinary retention	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-
Shivering	0 (0%)	0 (0%)	0 (0%)	1 (3.33%)	1.000; NS
Pruritus	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-
Hypotension	0 (0%)	1 (3.33%)	1 (3.33%)	4 (13.33%)	0.200; NS
Bradycardia	1 (3.33%)	0 (0%)	2 (6.67%)	2 (6.67%)	0.809; NS
Respiratory depression	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-

Limitations of the study

Our study was limited to30 patients a study in larger population may provide more detailed data on primary out come on duration of analgesia and other side effects. Dose adjustments of nalbuphine can produce errors in intrathecal dose.

Conclusion

- Nalbuphine provide very good quality of analgesia and prolongs duration of analgesia intraoperative and postoperative period
- Adverse effects of Nalbuphine are minimal and well manageable.
- It provides stable hemodynamics
- It does not produce respiratory depression.
- Dosage up to 0.8mg of nalbuphine may be used without any major adverse effects.

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